

AMENDMENTS TO THE CLAIMS

1-88. (Canceled)

89. (Currently Amended) A method of discovering a desired two or higher order combination of compounds having the ability to affect a biological property of living cells in a way that is indicative of the potential for therapeutic efficacy in an animal, said method comprising the steps of:

(a) providing at least forty-nine unique combinations of at least seven different compounds,

(b) contacting each unique combination with living test cells under conditions that ensure that each contacting is segregated from the others,

(c) measuring or detecting said biological property of the test cells as an indication of the effect of each combination on the test cells,

(d) identifying combinations of compounds that have an effect on a property of the test cells that is indicative of the potential for therapeutic efficacy in an animal a combination that affects said biological property of the test cells in said way that is indicative of the potential for therapeutic efficacy, and

(e) at any time during said method, contacting each compound in the combination identified in step (d) with said living test cells and thereafter measuring or detecting said biological property of the test cells as an indication of the effect of each compound on the test cells, wherein the combination identified in step (d) constitutes said desired combination if the effect of the combination on said biological property of the test cells is greater than qualitatively or quantitatively superior to the effect of each compound, individually, on said biological property of the test cells.

90. (Previously Presented) The method of claim 89, wherein step (b) comprises sequentially contacting said combinations of compounds with said test cells.

91. (Previously Presented) The method of claim 89, wherein said detecting step (c) is performed by a cytoblot assay.

92. (Previously Presented) The method of claim 89, wherein said detecting step (c) is performed by a reporter gene assay.

93. (Previously Presented) The method of claim 89, wherein said detecting step (c) is performed by a fluorescence resonance energy transfer assay.

94. (Previously Presented) The method of claim 89, wherein said detecting step (c) is performed by detecting a fluorescent calcium-binding indicator dye.

95. (Previously Presented) The method of claim 89, wherein said detecting step (c) employs fluorescence microscopy.

96. (Previously Presented) The method of claim 89, wherein step (c) employs expression profiling.

97. (Previously Presented) The method of claim 89, wherein said cells are human cells.

98. (Previously Presented) The method of claim 89, wherein said cells are selected from the group consisting of cancer cells, immune cells, neurons, fibroblasts, bacterial cells, and fungal cells.

99. (Previously Presented) The method of claim 89, wherein step (b) is carried out using a robotics system.

100. (Previously Presented) The method of claim 89, wherein step (b) is carried out using microfluidics.

101. (Previously Presented) The method of claim 89, wherein step (b) is carried out using ink-jet printer technology.

102. (Previously Presented) The method of claim 89, wherein said compounds are selected from the group consisting of non-polymeric organic compounds, lipids, carbohydrates, peptides, inorganic compounds, and oligonucleotides.

103. (Previously Presented) The method of claim 89, wherein at least one of said compounds is employed in purified form.

104. (Previously Presented) The method of claim 103, wherein each of said compounds is employed in purified form.

105. (Previously Presented) The method of claim 89, wherein said compounds are provided as components of mixtures.

106. (Previously Presented) The method of claim 105, wherein said mixtures are natural product extracts.

107. (Previously Presented) The method of claim 89, wherein said effect is a synergistic effect.

108. (Previously Presented) The method of claim 89, wherein at least one of said compounds is a molecule with a molecular weight of less than 1500 g/mole.

109. (Previously Presented) The method of claim 108, wherein said molecule is an FDA-approved drug.

110. (Previously Presented) The method of claim 108, wherein each of said compounds is a molecule with a molecular weight of less than 1500 g/mole.

111. (Previously Presented) The method of claim 110, wherein said each of said compounds are FDA-approved drugs.

112. (Previously Presented) The method of claim 89, wherein each of said combinations screened for biological activity is a two-compound combination.

113. (Previously Presented) The method of claim 89, wherein each of said combinations screened for biological activity is a three-compound combination.

114. (Previously Presented) A method of discovering a desired two or higher order combination of compounds having the ability to affect a biological property of living cells in a way that is indicative of the potential for therapeutic efficacy in an animal, said method comprising the steps of:

- (a) providing at least two hundred unique combinations of at least seven different compounds,
- (b) contacting each unique combination with living test cells under conditions that ensure that each contacting is segregated from the others,
- (c) measuring or detecting said biological property of the test cells as an indication of the effect of each combination on the test cells,
- (d) identifying combinations of compounds that have an effect on a property of the test cells that is indicative of the potential for therapeutic efficacy in an animal a combination that affects said biological property of the test cells in said way that is indicative of the potential for therapeutic efficacy, and
- (e) at any time during said method, contacting each compound in the combination identified in step (d) with said living test cells and thereafter measuring or detecting said biological property of the test cells as an indication of the effect of each compound on the test cells, wherein the combination identified in step (d) constitutes said desired combination if the effect of the combination on said biological property of the test cells is greater than qualitatively or quantitatively superior to the effect of each compound, individually, on said biological property of the test cells.

115. (Previously Presented) The method of claim 114, wherein step (b) comprises sequentially contacting said compounds with said test cells.

116. (Previously Presented) The method of claim 114, further comprising the step of (f) repeating step (a) through (e) at least twice, wherein, in step (b), said contacting of at least 200 combinations is different in each repetition.

117. (Previously Presented) The method of claim 116, wherein at least two repetitions of step (f) occur within 10 days of each other.

118. (Previously Presented) The method of claim 114, wherein said contacting step (b) comprises contacting at least 400 unique two or higher order combinations of compounds and said compounds individually with living test cells.

119. (Previously Presented) The method of claim 114, wherein said contacting step (b) comprises contacting at least 1540 unique two or higher order combinations of compounds and said compounds individually with living test cells.

120. (Previously Presented) The method of claim 114, wherein said compounds are selected from the group consisting of non-polymeric organic compounds, lipids, carbohydrates, peptides, inorganic compounds, and oligonucleotides.

121. (Previously Presented) The method of claim 114, wherein at least one of said compounds is employed in purified form.

122. (Previously Presented) The method of claim 114, wherein each of said compounds is employed in purified form.

123. (Previously Presented) The method of claim 114, wherein said compounds are provided as components of mixtures.

124. (Previously Presented) The method of claim 123, wherein said mixtures are natural product extracts.

125. (Previously Presented) The method of claim 114, wherein said effect is a synergistic effect.

126. (Previously Presented) The method of claim 114, wherein step (b) is carried out using a robotics system.

127. (Previously Presented) The method of claim 114, wherein step (b) is carried out using microfluidics.

128. (Previously Presented) The method of claim 114, wherein step (b) is carried out using ink-jet printer technology.

129. (Previously Presented) The method of claim 114, wherein at least one of said compounds is a molecule with a molecular weight of less than 1500 g/mole..

130. (Previously Presented) The method of claim 129, wherein said molecule is an FDA-approved drug.

131. (Previously Presented) The method of claim 129, wherein each of said compounds is a molecule with a molecular weight of less than 1500 g/mole.

132. (Previously Presented) The method of claim 131, wherein said small compounds are FDA-approved drugs.

133. (Previously Presented) The method of claim 114, wherein each of said combinations screened for biological activity is a two-compound combination.

134. (Previously Presented) The method of claim 114, wherein each of said combinations screened for biological activity is a three-compound combination.

135. (Currently Amended) A method of discovering a desired two or higher order combination of compounds having the ability to affect a biological property of living cells in a way that is indicative of the potential for therapeutic efficacy in an animal, said method comprising the steps of:

- (a) providing at least forty-nine unique combinations of at least seven different compounds,
- (b) contacting each unique combination with living test cells under conditions that ensure that each contacting is segregated from the others,
- (c) measuring or detecting said biological property of the test cells as an indication of the effect of each combination on the test cells,
- (d) identifying combinations of compounds that have an effect on a property of the test cells that is indicative of the potential for therapeutic efficacy in an animal a combination that affects said biological property of the test cells in said way that is indicative of the potential for therapeutic efficacy,
- (e) at any time during said method, contacting each compound in the combination identified in step (d) with said living test cells and thereafter measuring or detecting said biological property of the test cells as an indication of the effect of each compound on the test cells, wherein the combination identified in step (d) constitutes said desired combination if the effect of the combination on said biological property of the test cells is greater than qualitatively or quantitatively superior to the effect of each compound, individually, on said biological property of the test cells, and
- (f) repeating steps (a) through (e) at least 25 times over a one-week period, using different combinations of compounds in each repetition.

136. (Previously Presented) The method of claim 135, wherein steps (a) through (e) are repeated at least 100 times over a 30-day period, using different combinations of compounds in each repetition.

137. (Previously Presented) The method of claim 135, wherein said compounds are selected from the group consisting of non-polymeric organic compounds, lipids, carbohydrates, peptides, inorganic compounds, and oligonucleotides.

138. (Previously Presented) The method of claim 135, wherein said compounds are employed in purified form.

139. (Previously Presented) The method of claim 135, wherein said compounds are provided as components of mixtures.

140. (Previously Presented) The method of claim 139, wherein said mixtures are natural product extracts.

141. (Previously Presented) The method of claim 135, wherein said effect is a synergistic effect.

142. (Previously Presented) The method of claim 135, wherein step (b) is carried out using a robotics system.

143. (Previously Presented) The method of claim 135, wherein step (b) is carried out using microfluidics.

144. (Previously Presented) The method of claim 135, wherein step (b) is carried out using ink-jet printer technology.

145. (Previously Presented) The method of claim 135, wherein at least one of said compounds is a molecule with a molecular weight of less than 1500 g/mole.

146. (Previously Presented) The method of claim 145, wherein said molecule is an FDA-approved drug.

147. (Previously Presented) The method of claim 145, wherein each of said compounds is a molecule with a molecular weight of less than 1500 g/mole.

148. (Previously Presented) The method of claim 147, wherein said compounds are FDA-approved drugs.

149. (Currently Amended) A method of discovering a desired two or higher order combination of compounds having the ability to affect a biological property of living cells in a way that is indicative of the potential for therapeutic efficacy in an animal, said method comprising the steps of:

- (a) providing at least ten thousand unique combinations of at least seven different compounds,
- (b) contacting each unique combination with living test cells under conditions that ensure that each contacting is segregated from the others,
- (c) measuring or detecting said biological property of the test cells as an indication of the effect of each combination on the test cells,
- (d) identifying combinations of compounds that have an effect on a property of the test cells that is indicative of the potential for therapeutic efficacy in an animal a combination that affects said biological property of the test cells in said way that is indicative of the potential for therapeutic efficacy,
- (e) at any time during said method, contacting each compound in the combination identified in step (d) with said living test cells and thereafter measuring or detecting said biological property of the test cells as an indication of the effect of each compound on the test cells, wherein the combination identified in step (d) constitutes said desired combination if the effect of the combination on said biological property of the test cells is greater than qualitatively or quantitatively superior to the effect of each compound, individually, on said biological property of the test cells, and
- (f) repeating steps (a) through (e) at least twice over a period of ten days or less, wherein, in step (a), said step of providing at least ten thousand unique combinations of at least seven different compounds is different in two or more repetitions.

150. (Previously Presented) The method of claim 149, wherein at least one of said compounds is a molecule with a molecular weight of less than 1500 g/mole.

151. (Previously Presented) The method of claim 150, wherein said molecule is an FDA-approved drug.

152. (Previously Presented) The method of claim 150, wherein each of said compounds is a molecule with a molecular weight of less than 1500 g/mole.

153. (Previously Presented) The method of claim 152, wherein said compounds are FDA-approved drugs.

154. (Previously Presented) A method of discovering a desired two or higher order combination of compounds having the ability to affect a biological property of living cells in a way that is indicative of the potential for therapeutic efficacy in an animal, said method comprising the steps of:

- (a) contacting living test cells with at least 100 compounds under conditions that ensure that each compound/test cell contacting is segregated from the others,
- (b) detecting or measuring a biological property of said test cells,
- (c) selecting compounds that cause a change in said biological property relative to said biological property of said test cells not contacted with said compounds,
- (d) contacting at least 49 unique two or higher order combinations of the selected compounds of step (c) with living test cells under conditions that ensure that each contacting is segregated from the others,
- (e) detecting or measuring a biological property of said test cells of step (d), and
- (f) identifying combinations of compounds that cause an effect on said biological property of said test cells that is different from the effect of each compound of the combination by itself, wherein said identified combinations of compounds have potential therapeutic use in an animal.

155. (Previously Presented) The method of claim 154, wherein the test cells of step (a) are the same as the test cells of step (d).

156. (Previously Presented) The method of claim 154, wherein the biological property of step (b) is the same as the biological property of step (d).